

CLAIMS

1. A probe for detecting an agonist or an antagonist to a nuclear receptor, in which, at least, a ligand-recognition site containing a
5 ligand-binding domain of the nuclear receptor is connected with a binding-responsive site containing a peptide chain that specifically binds to a coactivator-binding site in the ligand-binding domain by a flexible linker to construct a fusion structure [ligand-recognition
10 site/linker/binding-responsive site], and two reporters are connected with the respective ends of the fusion structure.

2. The probe of claim 1, wherein the ligand-recognition site contains a ligand-binding domain of a nuclear receptor selected from the group including glucocorticoid receptor, estrogen receptor, progesterone
15 receptor, peroxisome proliferator-activated receptor, androgen receptor, thyroid gland hormone receptor, retinoic acid receptor, vitamin D receptor and orphan receptors.

3. The probe of claim 1, wherein the ligand-recognition site is
20 an estrogen receptor α ligand-binding domain, a peroxisome growth factor activation receptor ligand-binding domain or an androgen receptor ligand-binding domain.

4. The probe of claim 3, wherein the binding-responsive site is
25 a nuclear receptor interaction domain peptide of steroid receptor coactivator 1.

5. The probe of claim 3, wherein the binding-responsive site contains the motif of SEQ ID No: 1.

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6. The probe of any of claims 1 to 5, wherein the two reporters are a yellow fluorescent protein and a cyan fluorescent protein.

7. A method for screening an agonist to nuclear receptor,
5 which comprises making any of the probes of claims 1 to 6 coexist with an agonist candidate substance, and measuring changes in signals with and without the agonist candidate substance.

8. The method for screening an agonist according to claim 7,
10 wherein the probe coexists with the agonist candidate substance in cells by introducing a polynucleotide expressing the probe into the cells.

9. The method for screening an agonist according to claim 7,
wherein the probe coexists with the agonist candidate substance in all cells
15 of a non-human animal or its progeny by introducing a polynucleotide expressing the probe into a non-human animal totipotent cell and developing the cell into a individual animal.

10. A method for screening an antagonist to nuclear receptor,
20 which comprises making any of the probes of claims 1 to 6 coexist with an excessive amount of antagonist candidate substance and a known agonist, and measuring changes in a signal with and without the antagonist candidate substance.

25 11. The method for screening an antagonist according to claim 10, wherein the probe coexists with the agonist and the antagonist candidate substance in cells by introducing a polynucleotide expressing the probe into the cells.

30 12. The method for detecting an antagonist according to claim

10, wherein the probe coexists with the agonist and the antagonist candidate substance in all cells of a non-human animal or its progeny by introducing a polynucleotide expressing the probe into a non-human animal totipotent cell and developing the cell into an individual animal.

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13. A non-human animal or its progeny, which is established by introducing a polynucleotide expressing any of the probes of claims 1 to 6 into non-human animal totipotent cell and developing the cell into an individual animal.

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